Nkx6-1 controls the identity and fate of red nucleus and oculomotor neurons in the mouse midbrain.

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Scientific Abstract:
Little is known about the cues controlling the generation of motoneuron populations in the mammalian ventral midbrain. We show that Otx2 provides the crucial anterior-posterior positional information for the generation of red nucleus neurons in the murine midbrain. Moreover, the homeodomain transcription factor Nkx6-1 controls the proper development of the red nucleus and of the oculomotor and trochlear nucleus neurons. Nkx6-1 is expressed in ventral midbrain progenitors and acts as a fate determinant of the Brn3a(+) (also known as Pou4f1) red nucleus neurons. These progenitors are partially dorsalized in the absence of Nkx6-1, and a fraction of their postmitotic offspring adopts an alternative cell fate, as revealed by the activation of Dbx1 and Otx2 in these cells. Nkx6-1 is also expressed in postmitotic Isl1(+) oculomotor and trochlear neurons. Similar to hindbrain visceral (branchio-) motoneurons, Nkx6-1 controls the proper migration and axon outgrowth of these neurons by regulating the expression of at least three axon guidance/neuronal migration molecules. Based on these findings, we provide additional evidence that the developmental mechanism of the oculomotor and trochlear neurons exhibits more similarity with that of special visceral motoneurons than with that controlling the generation of somatic motoneurons located in the murine caudal hindbrain and spinal cord.